DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

APR 29 1999

NDA 19-627/S-031

Zeneca Pharmaceuticals
1800 Concord Pike
PO Box 15437
Wilmington, Delaware 19850-5437

Attention: William J. Kennedy, Ph.D.
Vice President, Drug Regulatory Affairs

Dear Dr. Kennedy:

Please refer to your supplemental New Drug Application (sNDA) dated March 09, 1998, received March 10, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diprivan (propofol) Injectable Emulsion.

We note that this supplement was submitted as "Special Supplement-Changes Being Effected" under 21 CFR 3 14.70 (c) (2) (i).

This supplemental New Drug Application (sNDA) provides for the addition of a **"Geriatric Use"** subsection in the labeling ", as per the "Geriatric Use" Final Rule.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted labeling (package insert submitted March 9, 1998) with the revision listed below. Accordingly, the supplemental application is approved effective on the date of this letter.

The agency's additional text to be added as paragraph one under "Precaution" is denoted by underlining.

PRECAUTIONS
Geriatric use: The effect of age on induction dose requirements for propofol was assessed in an open study involving 211 unpremedicated patients with approximately 30 patients in each decade between the ages of 16 and 80. The average dose to induce anesthesia was calculated for patients UP to 54 years of age and for patients 55 years of age or older.The average dose to induce anesthesia in patients up to 54 years of age was 1.99 mg/kg and in patients above 54 it was 1.66 mg/kg Subsequent clinical studies have demonstrated lower dosing requirements for subjects greater than 60 years of age.

This revision is the term of the supplemental approval

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 19-627/S-0 31." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 3 14.80 and 3 14.81.

If you have any questions, contact David Morgan, Regulatory Project Manager, at (301) 827-74 10.

Sincerely,

Cynthia McCormick MD

G. McCormick, M.D.
Director
Division of Anesthetic, Critical Care,
and Addiction Drug Products, HFD- 170
Office of Drug Evaluation III
Center for Drug Evaluation and Research